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In the claims

Please cancel claims 29-32 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

Please amend the claims pursuant to the provisions of proposed new rule 121 as described in the Official Gazette on February 25, 2003, as follows:

1. (Twice Amended) A method for detecting a molecule ~~in contact with~~ which is labeled with a second harmonic-active label at an interface, which comprises:

(a) ~~contacting an the labeled molecule with the interface with a molecule which comprises a second harmonic-active label attached to the molecule; and~~

(b) detecting light emitted from the interface using a surface selective technique so as to detect the ~~second harmonic-active~~ labeled molecule in contact with the interface,

*b1*  
~~wherein the molecule is not detectable in contact with the interface using the surface selective technique in the absence of the second harmonic-active label~~ an unlabeled molecule at the interface is undetectable using the surface selective technique.

2. The method of claim 1, wherein the surface selective technique is second harmonic generation or sum-frequency generation.

3. The method of claim 1, wherein the molecule is a protein, a nucleic acid, a lipid, or a carbohydrate.

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4. The method of claim 3, wherein the nucleic acid is a ribonucleic acid (RNA) or a deoxyribonucleic acid (DNA).
5. The method of claim 1, wherein the molecule is a pollutant.
6. The method of claim 1, wherein the molecule is on a surface of a nanoparticle or a polymer bead.
7. (Previously Amended) The method of claim 1, wherein the second harmonic-active label is bound to the molecule by a specific interaction or a non-specific interaction.
8. The method of claim 7, wherein the specific interaction comprises a covalent bond or a hydrogen bond.
9. The method of claim 7, wherein the non-specific interaction comprises an electrostatic interaction.
10. (Previously Amended) The method of claim 1, wherein the second harmonic-active label is specific for an amine group or a sulfhydryl group on the molecule.
11. (Previously Amended) The method of claim 1, wherein the second harmonic-active label comprises a plurality of individual second harmonic-active moieties which each have a nonlinear susceptibility and are bound together in a fixed and determinate orientation with respect to each other so as to increase the overall nonlinear susceptibility of the second harmonic-active label.
12. The method of claim 1, wherein the interface is at a membrane, a liposome, a cell surface, a viral surface, a bacterial surface, or a biosensor.
13. The method of claim 1, wherein the interface is a vapor-

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liquid interface, a liquid-liquid interface, a liquid-solid, or a solid-solid interface.

14. The method of claim 13, wherein the vapor-liquid interface is an air-water interface.
15. The method of claim 13, wherein the liquid-liquid interface is an oil-water interface.
16. The method of claim 13, wherein the liquid-solid interface is a water-glass interface or a benzene-SiO<sub>2</sub> interface.
17. (Previously Amended) The method of claim 1, wherein the molecule is a protein and the interface is at a receptor on a membrane.
18. (Previously Amended) The method of claim 1, wherein the molecule is on a viral surface and the interface is at a cell surface.
19. (Previously Amended) The method of claim 1, wherein the molecule is a protein and the interface is at a protein.
20. (Previously Amended) The method of claim 1, wherein the molecule is on a cell and the interface is at a cell surface.
21. (Twice Amended) A method for detecting a molecule in a medium, which comprises:
  - (a) labeling a surface with a first molecule which ~~comprises~~ is labeled with a second harmonic-active label ~~attached to the molecule~~, wherein the ~~second harmonic-active label~~ first molecule specifically interacts with a second molecule to be detected, and

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~~wherein the second harmonic active labeled molecule is not detectable at the surface using the surface selective technique in the absence of the second harmonic active label,~~

- (b) contacting the surface with a medium comprising the second molecule, thereby creating an interface at the surface,
  - (c) detecting the ~~second harmonic active labeled~~ first molecule at the interface by measuring a signal generated using a surface selective technique, wherein an unlabeled molecule at the interface is undetectable using the surface selective technique, and
  - (d) detecting a change in the signal when the second molecule interacts with the ~~second harmonic active labeled~~ first molecule, thereby detecting the second molecule in the medium.
22. The method of claim 21, wherein the surface is on a nanoparticle or a polymer bead.
23. The method of claim 21, wherein the surface selective technique is second harmonic generation or sum-frequency generation.
24. The method of claim 21, wherein the molecule is a pollutant or a charged species.
25. The method of claim 24, wherein the pollutant is lead or polychlorinated biphenyl.
26. The method of claim 24, wherein the charged species is a chloride ion.

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27. (Previously Amended) The method of claim 21, wherein the interaction between the second harmonic-active labeled molecule and the molecule to be detected is an antibody-antigen interaction.
28. (Previously Amended) The method of claim 21, wherein the medium contains an amount of the molecule to be detected, the change in the signal when the molecule interacts with the second harmonic-active labeled molecule is a quantitative change, and the amount of the molecule in the medium can be determined from the change in the signal.
29. (Canceled) ~~A method for determining the orientation of a molecular species within a planar surface, which comprises:~~  
~~(a) labeling the species with a second harmonic active moiety which specifically binds to the species;~~  
~~(b) determining the orientation of the second harmonic active moiety with respect to the species;~~  
~~(c) measuring the polarization of second harmonic light to determine the orientation of the second harmonic active moiety with respect to the planar surface, and~~  
~~determining the orientation of the species within the planar surface from the orientation of the moiety with respect to the surface as determined in step (c) and from the orientation of the moiety with respect to the species as determined in step (b).~~
30. (Canceled) ~~The method of claim 29, wherein the orientation of the second harmonic active moiety with respect to the species is determined using x-ray crystallography.~~
31. (Canceled) ~~The method of claim 29, wherein the planar~~
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~~surface is selected from the group consisting of an organic material surface, an inorganic material surface, a polymeric material surface, a mineral surface, a clay surface, a biological membrane surface, and a synthetic membrane surface.~~

32. (Canceled) ~~The method of claim 29, wherein the molecular species is selected from the group consisting of an organic species, an inorganic species, a polymeric species, a protein, a lipid, a nucleic acid, and a carbohydrate.~~
33. The method of claim 21, wherein the molecule to be detected is labeled with a second harmonic-active label.
34. (Amended) A method for detecting an interaction between a first labeled molecule which is labeled with a second harmonic-active label and a second molecule, which comprises:
- (a) contacting a the first labeled molecule at an interface with a medium comprising a the second molecule, ~~wherein said first labeled molecule comprises a second harmonic-active label attached to the molecule, wherein the second harmonic-active label~~ first molecule specifically interacts with the second molecule, ~~and wherein the first molecule is not detectable at the interface using a surface selective technique in the absence of the second harmonic active label;~~ and
- (b) detecting an interaction ~~of said~~ between the first molecule and the second molecule with said first labeled molecule at said at the interface by measuring a signal generated using a surface selective technique, wherein an unlabeled molecule at the
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interface is undetectable using the surface selective technique.

35. The method of claim 34, wherein said second molecule is labeled with a second harmonic-active label.
36. (Amended) The method of claim 21, wherein the first molecule or the second molecule is selected from the group consisting of a lipid, carbohydrate, protein and nucleic acid.
37. (Amended) The method of claim 34, wherein the first molecule or the second molecule is selected from the group consisting of a lipid, carbohydrate, protein and nucleic acid.
38. (New) The method of claim 1, wherein the interface is a cell surface and the labeled molecule is prepared outside of the cell.
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